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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,942	06/21/2001	Juha Punnonen	0179.210US	4876

7590 08/24/2005

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EXAMINER
AKHAVAN, RAMIN

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/886,942	PUNNONEN ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 3-4, 7-8, 10-11, 14-18, 21-23, 26-28, 31, 33, 35-36, 44, 46-48, 62-66, 74-79, 93-94, 106-107, 113-116, 118-126* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *See Continuation Sheet* is/are allowed.

6)☒ Claim(s) *3,8,14-18,120 and 123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1.52

DETAILED ACTION

Receipt is acknowledged of a response filed 04/18/2005. Claims 2, 5-6, 9, 12-13, 19-20, 24-25, 29-30, 32, 34, 37-43, 45, 49-61, 67-73, 80-92, 95-105, 108-112, and 117 are canceled. Further, claims 1, 3, 7-8, 10, 21-23, 26-28, 31, 33, 35-36, 44, 46, 62, 65, 74, 93, 106, 1 13-116, and 118-119 are amended. Thus, claims 1, 3-4, 7-8, 10-11, 14-18, 21-23, 26-28, 31, 33, 35-36, 44, 46-48, 62-66, 74-79, 93-94, 106-107, 113-116, 118-126 are pending in this application.

All objections/rejections not repeated herein are hereby withdrawn. Where applicable, a response to Applicant's arguments will be set forth immediately following the body of any objections/rejections repeated herein. As no new grounds of rejection are set forth that were not necessitated by amendment to the claims, **this action is made FINAL**.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Claims 3, 8, 14-18, 120 and 123 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.**

This rejection is of record and repeated herein in salient part. It is new ground of rejection as applied to new claims 120 and 123, which rejection is necessitated by amendment to the claims. A response to Applicant's argument is set forth immediately below. (Infra, Response to Arguments).

The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As amended, the claims are directed to a genus of nucleic acid molecules that comprise a promoter sequence that is at least 99% identical to SEQ ID NO: 8 (1.767 kb in length), or with respect to claims 120 and 123 99.5%. Thus, at least 17 (99%) or 9 (99.5%) nucleotide alterations can be made anywhere within SEQ ID NO: 8. If the number of potential alterations were narrowed to 1 nucleotide, there would be 1,767 potential alterations. It follows that the potential number of embodiments encompassed by said genus of promoter sequences is in the tens to hundreds of thousands, wherein each embodiment must meet the aforementioned structural identity to SEQ ID NO: 8, while concomitantly corresponding to the functional limitation relative to the reference CMV promoters.

Applicant's specification teaches a "shuffling" method for generating and identifying promoter sequences with desired promoter activity, wherein similar sequences are randomly shuffled to produce novel sequences that are then screened for activity. For example, 4 different CMV templates are utilized in a shuffling protocol. (See, Specification, pp. 60-61, Example 1). The instant disclosure teaches how to screen a library of *shuffled* sequences to identify promoters having a desired level of activity. (e.g., Figures 2-3). For example, SEQ ID NO: 8 exihibits about 2-fold greater promoter activity than the reference promoters. (Figure 5, clone 6a8). However, as the disclosure makes clear, differential levels of activity are also generated relative to the shuffled library of promoter sequences, with the salient point being that said promoters have a

relatively few nucleotide changes. (e.g., differential activities observed in Figures 3 and 5 with corresponding sequences in Figure 8). Notably, the disclosure does not provide a means for envisaging a sufficient number of embodiments comprising the structural requirements relative to SEQ ID NO: 8 that will also retain the requisite level of activity to the reference promoters.

The evidence in the art supports the contention that the addition or absence of specific sequences within a CMV promoter can greatly alter function. (e.g., Chapman et al., p. 3982, col. 2, last ¶; reference of record; teaching differential CMV promoter activity based on the presence of about a 400 nucleotide sequence 5' of the first intron of the CMV promoter compared to smaller nucleic acids lacking the upstream region).

Given the vast size of the claimed genus of nucleic acid sequences that must correspond to the requisite functionality of equal or greater promoter activity as compared to reference CMV promoters, evidence in the prior art, the fact that even small changes within the core CMV IE promoter region can result in differential levels of promoter activity, and the lack of a means to envisage a sufficient number of embodiments that meet the functional limitations of the claims, the skilled artisan would not have been able to envisage a sufficient number of specific embodiments embraced by the claims to describe the broadly claimed genus of nucleic acid structures. Therefore, the artisan would reasonably have concluded applicants were not in possession of the claimed genus of nucleic acid structures.

Response to Arguments

Applicant's arguments filed 04/18/2005 have been fully considered but they are not persuasive.

In essence, Applicant asserts the following: (1) predictability of functionality corresponding to the encompassed nucleic acid structures is not the appropriate legal standard; and (2) the disclosure provides sufficient description of the relevant structural and functional characteristics of the claimed genus of nucleic acid structures, including common structural attributes corresponding to the requisite functionality. In support for the arguments, Applicant cites various case law that explicate the written description standard, which is not disputed herein. It is agreed that the issue is whether the instant disclosure provides sufficient description of a common structural attribute corresponding to the requisite functionality for the embodiments encompassed by the claimed genus of nucleic acid structures.

Regarding predictability of function relative to embodiments within a claimed genus, it is respectfully asserted that predictability is a valid consideration in determining whether Applicant is in possession of the claimed genus. Put another way, the more unpredictable the result regarding a claimed functionality for various species within the claimed genus, the more substantial the written description requirement with respect the essential or critical features of the invention.

For inventions in unpredictable technologies, or for inventions characterized by factors not reasonably predictable, which are known to one of ordinary skill in the art, more evidence is required to show possession. For example, disclosure of only a method of making the invention and the function may not be sufficient to support a product claim. See, e.g., *Fiers v. Revel*, 984 F.2d 1164, 1169, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993); *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).

In such instances the alleged conception fails the written description requirement not merely because the field is unpredictable or because of the general uncertainty surrounding experimental sciences, but because the conception is incomplete due to factual uncertainty that undermines the specificity of the inventor' s idea of the invention. *Burroughs Wellcome Co. v. Barr Laboratories Inc.*, 40 F.3d 1223, 1229, 32 USPQ2d 1915, 1920 (Fed. Cir. 1994).

Moreover, each claim is examined and must satisfy the written description requirement. Thus, a dependent claim can fail where the base claim meets the written description requirement. As the Guidelines for Written Description state "The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art" (Federal Register/ Vol. 66, No. 4/ Friday, January 5, 2001/Notices, column 1, page 1105). The Guidelines further state, "[t]he claim as a whole, including all limitations found in the preamble, the transitional phrase, and the body of the claim, must be sufficiently supported to satisfy the written description requirement" (at page 1105, center column, third full paragraph). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. *Lockwood v. American Airlines Inc.* (CA FC) 41 USPQ2d 1961 (at 1966).

Here, the critical or essential element is the nucleic acid sequence that corresponds to equal or greater promoter activity as compared to the reference CMV promoters. As the instant specifications makes clear there is unpredictability with respect to said sequences and the requisite functionality.

It follows that the greater the level of unpredictability amongst the various embodiments, then the greater the requirement for the disclosure to identify a common structure or provide a sufficient number of species within the genus, which advances the discussion to Applicant's second argument.

The nuclei acid structure of SEQ ID NO: 8 is the only structure that is common to all the embodiments within the claimed genus of promoters having the requisite functionality. As stated previously and herein above, there is unpredictability amongst the various structures that are defined by the common structure of SEQ ID NO: 8 *and* that must correspond to the relative promoter functionality. Indeed, evidence in Applicant's own disclosure makes clear that even a few nucleotide changes result in differential promoter activity, whether reduced, equal or greater than the reference promoters. (Figures 3, 5 and 8). Therefore, the written description requirement is not met, first, because the only common structure confers unpredictability of results regarding promoter function, and second, because the disclosed embodiments exhibit differential promoter activity undoubtedly borne from the aforementioned unpredictability.

In view of the foregoing, it is deemed that one of skill cannot conclude that Applicant is in possession of the claimed genus. Thus, the rejection is maintained.

Conclusion

Claims 3, 8, 14-18, 120 and 123 are rejected. Claims 1, 4, 7, 10-11, 21-23, 26-28, 31, 33, 35-36, 44, 46-48, 62-66, 74-79, 93-94, 106-107, 113-116, 118-119, 121-122 and 124-126 are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached between 8:30-5:00, Monday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD, can be reached on 571-272-0781. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully submitted,

Ray Akhavan/AU 1636

DAVID GUZO
PRIMARY EXAMINER

Continuation of Disposition of Claims: Claims allowed are 1,4,7,10,11,21-23,26-28,31,33,35,36,44,46-48,62-66,74-79,93,94,106,107,113-116,118,119,121 and 122.